18. URINARY TRACT INFECTION
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The general approach to urinary tract infections (UTIs) was obtained from one ambulatory medical text chapter (Barker et al., 1991), a textbook of diagnostic strategies (Panzer et al., 1991), and review articles which dealt with diagnosis and management of urinary tract infections. The review articles were chosen from a MEDLINE search which identified all English language review articles on urinary tract infection between the years of 1990 and 1995. Further, since the main controversy in UTIs concerns laboratory testing and therapy, we selected and reviewed references from the review articles which related to laboratory testing and antibiotic therapy. Finally, we performed another MEDLINE search (1990-1995) to identify any randomized controlled trials (RCTs) regarding treatment of UTIs.

IMPORTANCE
UTIs are among the most common bacterial infections seen by physicians and are the most common bacterial infection in women (Winickoff et al., 1981). They affect 10-20 percent of women in the United States annually and account for over 5 million office visits per year. Outpatient expenditures for patients with UTIs in the United States approach $1 billion (Powers, 1991).

Efficacy and/or Effectiveness of Interventions

Screening
There is no role for screening for UTIs for bacteriuria in otherwise healthy non-pregnant women under age 50 (Pels et al., 1989).

Diagnosis
The diagnosis of UTI is suggested by the history. An uncomplicated UTI is suggested by symptoms of bladder irritation and occasionally hematuria. An upper tract infection is suggested by the concomitant presence of fever, chills, and/or back pain. In addition, vaginal
infections (due to candida and trichomonas) and urethritis (due to Chlamydia trachomatis, Neisseria gonorrhoeae, or herpes simplex virus) could present with UTI-type symptoms. Therefore, a history of vaginal discharge and sexual activity should be sought. Since pregnant patients and those with diabetes and immunosuppression are treated differently, the history should specifically include these questions (Barker et al., 1991).

The urinalysis is the most important initial study in the evaluation of a patient suspected of having a UTI by history. A negative urinalysis makes the diagnosis of UTI extremely unlikely (Barker et al., 1991). A specimen should be collected by the “clean-catch” method to minimize likelihood of contamination (Barker et al., 1991), or by catheterization when the “clean-catch” method is impossible. A finding by microscopic examination using a high-power lens of bacteria of more than seven white cells/mm³ in unspun urine or more than two white cells per high-power field in spun urine is consistent with an UTI. The leukocyte esterase test has a sensitivity for defining UTI (if the test is positive) of between 62 and 68 percent, with a positive predictive value of only 46-55 percent and a negative predictive value of 88-92 percent (Pfaller and Koontz, 1985). A nitrite test has a sensitivity of 35-85 percent and specificity of 92-100 percent for the presence of bacteria (Pappas, 1991). The leukocyte-esterase nitrite combination has a sensitivity of 79.2 percent, a specificity of 81 percent and a negative predictive value of 94.5 percent for specimens with ≥10⁵ CFU/ml (Pfaller and Koontz, 1985).

A combination of findings (i.e., bacteriuria, pyuria and a positive nitrite test) is more highly predictive for UTI (Bailey, 1995).

The criteria for appropriate use of a culture are shown in Table 18.1
Table 18.1
Criteria for Appropriate Use of Culture

A culture should be obtained in women who have:

• “several” (three or more) infections in the past year
• diabetes or immunocompromised state
• fever, chills and/or flank pain
• acute pyelonephritis
• structural or functional anomalies of the urinary tract
• symptoms for more than 7 days before presentation
• pregnancy
• uncertain clinical or urinalysis features
• a relapse of symptoms after initial treatment
• age older than 65
• had a recent hospitalization or invasive procedure


Treatment

Treatment currently rests with the appropriate use of antibiotics. A single-dose or a three-day course of an oral antimicrobial has been shown to eradicate approximately 90-95 percent of cases of uncomplicated UTI in young women. However, therapy for three days or longer was more effective than single-dose therapy in most trials and in a meta-analysis (Stamm and Hooton, 1993; Elder, 1992; Johnson and Stamm, 1989; Norrby, 1990). Seven-day regimens should be reserved for patients with “complicated lower tract infections” (See Table 18.2).
Table 18.2
Definition of Complicated Lower Tract Infections

- Diabetes or immunocompromised state
- Functional or structural anomaly of the urinary tract
- Symptoms for longer than 7 days
- Recent urinary tract infection
- Acute pyelonephritis or more than 3 urinary tract infections in past year
- Use of diaphragm
- Age older than 65
- Pregnancy

Sources: Stamm and Hooton, 1993; Johnson and Stamm, 1989.

Patients with mild to moderate acute uncomplicated pyelonephritis should be treated for 10-14 days as outpatients (Stamm et al., 1987). Severe pyelonephritis, with nausea and vomiting, or possible urosepsis, may require hospitalization, as does pyelonephritis in pregnancy.

In general, trimethoprim/sulfamethoxazole double strength (160 mg/800 mg) is the most effective first-line agent, with resistance in 5-15 percent of cases. It should be used unless there is documented resistance, allergy, or pregnancy. Amoxicillin and nitrofurantoin have higher rates of failure (Stamm and Hooton, 1993; Johnson and Stamm, 1989; Elder, 1992; Norrby, 1990). The use of quinolones, while effective (Stein et al., 1987; Hooton et al., 1991), should be reserved for patients with known resistance or allergy to other first-line agents to avoid unnecessary expense and the promotion of resistant strains (Sable and Scheld, 1993).

Follow-up

Experts disagree on necessity for follow-up. Some feel a follow-up culture is unnecessary if symptoms of uncomplicated UTI have resolved within 3 days of starting treatment (Stamm and Hooton, 1993; Patton et al., 1991; Winickoff et al., 1981; Schultz et al., 1984). Barker et al. (1991) stipulate that the urinalysis should be re-evaluated within 7 days if a single-dose regimen was utilized or within 4 weeks if a 7-10
days course was used even if symptoms have cleared. Most experts agree, however, that follow-up culture is indicated within 2 weeks of complicated cystitis or pyelonephritis (Stamm and Hooton, 1993).
### RECOMMENDED QUALITY INDICATORS FOR URINARY TRACT INFECTIONS

The following criteria apply to women under age 50 without diabetes or immunocompromise.

**Diagnosis**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
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<tbody>
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<td>1. In women presenting with dysuria, presence or absence of fever and flank pain should be elicited.</td>
<td>III</td>
<td>Barker et al., 1991; Powers, 1991</td>
<td>Alleviate pain and fever. Prevent sepsis. Prevent abscess formation.</td>
<td>Fever and flank pain increase probability of upper tract infection (pyelonephritis).</td>
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<td>2. In women presenting with dysuria, a history of vaginal discharge should be elicited.</td>
<td>III</td>
<td>Panzer et al., 1991; Barker et al., 1991</td>
<td>Alleviate dysuria. Prevent allergic reactions from antibiotics. Prevent antibiotic associated diarrhea and yeast vaginitis.</td>
<td>Dysuria may be caused by vaginitis (and rarely cervicitis) as well as UTI. By evaluating cause for dysuria, treatment for vaginitis may be initiated and avoidance of antibiotics for non-UTI causes can be accomplished.</td>
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<td>3. If a woman presents with dysuria and a complaint of vaginal discharge, a speculum exam and microscopic examination of discharge (if any) should be performed (e.g., KOH and saline wet mount).</td>
<td>III</td>
<td>Panzer et al., 1991</td>
<td>Alleviate dysuria. Prevent allergic reactions to antibiotics. Prevent antibiotic associated diarrhea and yeast vaginitis.</td>
<td>Dysuria may be caused by vaginitis (and rarely cervicitis) as well as UTI. By evaluating cause for dysuria, treatment for vaginitis may be initiated and avoidance of antibiotics for non-UTI causes can be accomplished. This is implied from recommendation regarding treatment.</td>
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<td>4. Women presenting with dysuria should be asked about the possibility of concurrent pregnancy (e.g., date of LMP) or be given a pregnancy test.</td>
<td>III</td>
<td>Panzer et al., 1991; Barker et al., 1991</td>
<td>Avoid spontaneous abortion.</td>
<td>Women who are pregnant and have UTI are at risk for spontaneous abortion. Treatment needs to be for a longer period of time and follow-up cultures are necessary to document eradication of infection.</td>
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<td>5. A urinalysis should be performed on women in whom urinary tract infection is suspected.</td>
<td>III</td>
<td>Johnson and Stamm, 1989; Panzer et al., 1991</td>
<td>Prevent allergic reactions from antibiotics. Prevent antibiotic-associated diarrhea and yeast vaginitis.</td>
<td>Urinalysis, if negative for white blood cells, rules out UTI and antibiotics do not need to be used.</td>
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<td>6. A urine culture should be obtained for women who have dysuria and any one of the following: a. “several” (three or more) infections in the past year b. diabetes or immunocompromised state c. fever, chills and/or flank pain d. diagnosis of pyelonephritis e. structural or functional anomalies of the urinary tract f. pregnancy g. a relapse of symptoms, or h. a recent hospitalization or invasive procedure.</td>
<td>III</td>
<td>Powers, 1991; Barker et al., 1991; Panzer et al., 1991</td>
<td>Alleviate dysuria. Prevent pyelonephritis. Prevent uti recurrence.</td>
<td>Appropriate and prompt treatment in these instances can prevent complications and recurrences. However, there is little empiric evidence to support the timing for obtaining a urine culture.</td>
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<td>7. If the patient has dysuria and a urinalysis shows more than 5 WBC per high-power field, the patient should receive treatment with antimicrobials.</td>
<td>II-2; III</td>
<td>Panzer et al., 1991; Barker et al., 1991</td>
<td>Prevent complications of untreated infection (including pyelonephritis from lower tract UTI, and PID, ectopic pregnancy and infertility from cervicitis).</td>
<td>Patients with pyuria and dysuria almost always have an infection that will respond to antimicrobial agents. This infection may not always be a UTI (for example, chlamydia urethritis can present with dysuria and pyuria). Treatment of UTI can prevent complications of upper tract infection and sepsis. Treatment of chlamydial infection can prevent future PID, ectopic pregnancies, and infertility. The number of WBC per high power field indicative of a UTI in centrifuged urine is usually given as 2-5. We have chosen the upper range.</td>
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<td>8. If a diagnosis of UTI (upper or lower tract) has been made, the patient should be treated with antimicrobial therapy.</td>
<td>III; II-2</td>
<td>Stamm and Hooton, 1993; Johnson and Stamm, 1989; Powers, 1991</td>
<td>Prevent complications of untreated infection.</td>
<td>Both upper and lower tract infections respond to a number of antimicrobial agents. Trimethoprim-sulfa is usually chosen as a first line agent. While no RCTs have shown benefits of treatment, it is recognized that treatment of both lower and upper tract infections is beneficial (see above).</td>
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<td>9. Trimethoprim-sulfamethoxazole should be used as a first-line agent in outpatients with uncomplicated lower tract infection unless there is: 1) documented history of allergy; 2) suspected drug resistance; or 3) pregnancy.</td>
<td>II-2; III</td>
<td>Johnson and Stamm, 1989; Carlson, 1985; Sable, 1993</td>
<td>Decrease dysuria. Prevent drug resistance.</td>
<td>This recommendation is based on studies of susceptibility of urinary tract infections to various antibiotics and costs, primarily reviewed in the Johnson and Stamm article. TMP-SMZ is the most effective antibiotic (least resistance, lower rates of recurrence). Fluoroquinolones, while equally effective, have a broader spectrum and casual use promotes resistance in the individual and population.</td>
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<td>10. Treatment with antimicrobials for uncomplicated lower tract infection should not exceed 7 days.</td>
<td>I; III</td>
<td>Stamm and Hooton, 1993; Johnson and Stamm, 1989; Elder, 1992; Fihn et al., 1988</td>
<td>Decrease dysuria. Prevent antibiotic allergic reactions. Prevent antibiotic associated diarrhea. Prevent antibiotic associated superinfections. Several studies, summarized in the review articles cited, have shown that one day therapy is effective but that it may increase relapse. A well conducted RCT by Fihn et al using TMP-Sulfa showed that although a 10 day tx yielded superior cure rate at 2 weeks, by 6 weeks the advantage had diminished. The adverse effects were higher in the 10 day group. Therefore, several experts advocate the 3-day regimen in absence of RCT data on the 3-day regimen. There is no evidence that the benefit of prolonged therapy outweighs the risk of antibiotic allergies, superinfection, diarrhea and constitutional symptoms.</td>
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<td>11. At least 10 days of antimicrobial therapy should be prescribed for a suspected upper tract infection (pyelonephritis).</td>
<td>III</td>
<td>Johnson and Stamm, 1989; Stamm and Hooton, 1993; Stamm et al., 1991</td>
<td>Decrease pain. Decrease fever. Prevent recurrence of UTI. Prevent complications (such as sepsis and abscess). In general, it is agreed that a longer duration of treatment is necessary for upper tract than lower tract infections. Untreated infections can lead to recurrence and abscess. There is some controversy about the need for 10 versus 14 days of treatment and studies have reached varying conclusions. The review by Johnson and Stamm indicates that there is not enough evidence to warrant treatment for less than 14 days, based on recurrence of infection. However, as this is an area of controversy, we have proposed at least 10 days of treatment.</td>
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<td>12. A patient with known or suspected upper tract infection who has uncontrolled vomiting in the office or ER should be hospitalized.</td>
<td>III</td>
<td>Stamm and Hooton, 1993</td>
<td>Decrease pain. Decrease fever. Prevent sepsis. If vomiting cannot be controlled in the office or ED, it is unlikely that the patient will be able to take oral medications at home. Some hospitals have provisions to administer IV antibiotics in the home.</td>
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<td>13. A pregnant patient with pyelonephritis should be hospitalized.</td>
<td>III</td>
<td>Stamm and Hooton, 1993</td>
<td>Prevent spontaneous abortion. Patients who are pregnant and have pyelonephritis are at risk for spontaneous abortion.</td>
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<td>14. Regimens of at least 7 days should be used for patients with complicated lower tract infections: those with: a. diabetes, b. functional or structural anomaly of the urinary tract, c. symptoms for longer than 7 days, d. recent urinary tract infection, e. use of diaphragm, and f. pregnancy.</td>
<td>III</td>
<td>Stamm and Hooton, 1993</td>
<td>Prevent recurrence of UTI. Prevent sepsis. Prevent abscess formation. Prevent spontaneous abortion. While there are no RCTs that demonstrate the optimal duration of treatment in these situations, a longer duration of treatment than for an uncomplicated lower tract infection is recommended because eradication is more difficult (i.e., in structural anomalies) and/or potential complications secondary to incomplete eradication are more serious (i.e., diabetes, pregnancy).</td>
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Follow-up

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<td>15. For upper tract infection or complicated lower tract infection, a repeat culture should be obtained within 2 weeks of finishing treatment.</td>
<td>III</td>
<td>Barker et al., 1991; Stamm and Hooton, 1993</td>
<td>Prevent recurrence of UTI.</td>
<td>Since eradication of organism is sometimes difficult in pyelonephritis and complicated lower tract infections, and incomplete eradication may lead to complications, a repeat culture is indicated.</td>
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Quality of Evidence Codes:
I: RCT
II-1: Nonrandomized controlled trials
II-2: Cohort or case analysis
II-3: Multiple time series
III: Opinions or descriptive studies
REFERENCES – URINARY TRACT INFECTION


